Immunisation after hepatitis B polyvalent vaccination among children in South Kivu Province, Democratic Republic of the Congo

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Background. The World Health Organization recommends the integration of vaccination against hepatitis B virus (HBV) into the national immunisation programmes of all highly endemic countries. Protective efficacy, defined as a hepatitis B surface antibody (HBsAb) level ≥10 mIU/mL, is ideally obtained in >90 - 95% of immunised children. The Democratic Republic of the Congo (DRC) implemented this recommendation in 2007 by introducing administration of hepatitis B vaccine in a combined formulation.
Objectives. To assess the rate of seroprotection in children who received hepatitis B vaccine in the DRC context.
Methods. This descriptive cross-sectional study was conducted during routine postnatal consultations at the General Hospital of Bukavu in South Kivu Province, DRC. A total of 200 infants aged 6 - 12 months and their mothers were consecutively enrolled. All the infants received the three-dose regimen of hepatitis B vaccine 6, 10 and 14 weeks after birth. The mothers were tested for hepatitis B surface antigen and HIV, while HBsAb levels were measured in the infants to determine immune response.
Results. Seroprotection was achieved in 84.5% of the infants. No maternal (age, parity, duration of pregnancy, HIV and HBV status) or infant (sex, weight at birth) factors were found to be associated with absence of immunological response.
Conclusions. The study demonstrated that the rate of seroprotection in the current vaccination programme against HBV in DRC was lower than desirable but comparable to rates reported in some other African countries. Further studies are needed to assess this finding and to evaluate ways to optimise the seroprotection rate.

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Hepatitis B virus (HBV) is a major health problem.[1,2] Globally more than 2 billion people have been infected with HBV, and according to World Health Organization (WHO) estimates, 257 million people were living with chronic HBV infection in 2015. Among them, 60 million were from Africa.[2-4] After perinatal transmission, one of the major modes of transmission in Africa, up to 90% of infected infants develop chronic infection with the risk of cirrhosis, liver failure, cancer and premature death.[2,5] Main routes of transmission are *in utero*, by exposure to blood or body fluids during birth, and horizontally during early life. Prevention of transmission of HBV from mother to child and during early life is therefore an important public health goal.

In 1992, the WHO recommended the integration of hepatitis B vaccination into the national immunisation programmes of highly endemic countries by 1995 and all other countries by 1997.[6] The vaccination schedule consists of three or four doses of hepatitis B vaccine and administration of HBV immunoglobulins to infants born to hepatitis B surface antigen (HBsAg)-positive mothers. In addition, the WHO recommended a first dose of hepatitis B vaccine within 24 hours of birth, especially in highly endemic countries (HBV prevalence >8%), with the objective of reducing the risk of early mother-to-child transmission.[7,8]

Hepatitis B vaccines are currently available not only in monovalent formulations but also in combinations that protect against HBV and several other diseases (e.g. diphtheria, tetanus and pertussis). Benefits of these combined vaccines include a reduction in the number of injections and the related cost, resulting in improved adherence to the vaccination programme. However, if immunisation against HBV begins at birth, only monovalent hepatitis B vaccine should be used, as the other antigens in combined vaccines are not approved for use at birth. For this reason, all combined vaccines are currently started 6 weeks after birth.[9]

In 2007, the Democratic Republic of the Congo (DRC) adopted and implemented a universal infant hepatitis B immunisation programme consisting of administration of three doses of this vaccine in a combined formulation. Since 2009, it has been provided as an active pentavalent vaccine against diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b and HBV (DTwP-Hib-HepB). The three doses of this vaccine are routinely administered to infants at the ages of 6, 10 and 14 weeks.[10]

Objectives

To evaluate the effect of hepatitis B vaccine in this combined formulation and to determine the rate of seroprotection in DRC, a country with a high prevalence of HBV.

Methodology

Population study

Blood from a convenience sample of 200 consecutive mother-child dyads was collected during routine postnatal consultations between

the 6th and 12th month of life at the General Hospital of Bukavu during 2014.

Data recorded included pregnancy information, maternal and infant characteristics and laboratory results (Table 1). Some of these variables were chosen because they have been associated with variations in response rates following hepatitis B vaccine administration.[11] In our study, mothers and infants were consecutively enrolled during routine visits for the immunisation schedule.[10] We included only infants who had received all three injections of hepatitis B vaccine according to their immunisation card. Infants who had not yet received the third dose were excluded.

Current immunisation schedule for children in DRC[10]

- At birth: BCG (tuberculosis), oral polio vaccine (OPV) dose 0
- At 6 weeks: OPV dose 1 and DTwP-Hib-HepB dose 1
- At 10 weeks: OPV dose 2 and DTwP-Hib-HepB dose 2
- At 14 weeks: OPV 3 and DTwP-Hib-HepB dose 3.

During the vaccination programme, anthropometric parameters of infants are monitored monthly up to 9 months.

Ethical considerations

The study design was approved by the Ethics Committee of the Catholic University of Bukavu, DRC (ref. no. UCB/CIE/NC/03B/2014). Informed consent was obtained from all mothers before blood samples were collected.

Serological analyses

Samples from the mothers were analysed using reagents Determine HBV HBsAg (Inverness Medical Japan Ltd, Japan) for HBV and Determine HIV 1/2 (Abbott Diagnostics, USA) for HIV. The results were classified as positive or negative according to the manufacturers' instructions. Subjects who were positive for HBsAg and HIV were considered to be carriers of both viruses. Determination of immune response in the infants was performed with a quantitative test (MONOLISA anti-HBs EIA; Bio-Rad Laboratories, USA) in the first 122 samples and with a qualitative reagent (HBs antibodies ELISA test; Autobio Diagnostics, China) in the last 78 samples for economic reasons and because the former test was no longer available. The qualitative test consisted of an immunochromatographic assay in which results are interpreted by visual observation.

An inter-laboratory comparison was undertaken to guarantee the quality of laboratory results by exchanging 30 maternal samples with the laboratory at St Luc Hospital, Brussels, Belgium, in which serological tests were performed using the cobas 6000 analyser series (Roche, Switzerland).

Analysis of the immune response

For quantitative tests, a level of hepatitis B surface antibody (HBsAb) ≥10 mIU/mL was considered a good immunological response according to the WHO criteria.[4] According to the qualitative test's instructions, positive tests were considered as responders and negative tests as non-responders.

Statistical analysis

Results were expressed as means (standard deviations (SDs)). Bivariate analyses comparing two subgroups of infants, responders and non-responders, in terms of sociodemographic characteristics and associated clinical factors were performed using Student's *t*-test. Differences between qualitative data were evaluated using the χ^2 test. Statistical significance was set at $p<0.05$. Analyses were performed using Statistical Package for Social Sciences (SPSS) software version 17.0 (IBM, USA).

Results

A total of 200 consecutive infants who had received the three doses of hepatitis B vaccine were screened for immune response to vaccination. Their mothers' characteristics are set out in Table 2. The mean (SD) age of the mothers was 29.3 (6) years and that of the infants 9.1 (2.4) months. Of the mothers, 97% had normal term pregnancies and 93% normal deliveries. No mother reported having been vaccinated against HBV, while the seroprevalences of HIV and HBsAg were 2% and 3%, respectively. The inter-laboratory comparison of these tests showed identical results between the two laboratories.

Of the infants, 19/122 in the group tested with the quantitative kit had an HBsAb level <10 mIU/mL and 12/78 were negative with the qualitative test, giving a total of 31 non-responders (15.5%) (Table 3).

Table 3 also outlines the maternal and infant characteristics in the responders and non-responders. Factors such as maternal age, gestational age, parity and maternal HBsAg/HIV status were not found to significantly affect HBsAb levels in infants receiving the three doses of hepatitis B vaccine.

No statistically significant differences in sex or infant's weight at birth were observed between responders and non-responders.

Discussion

We present the immunological response observed after universal hepatitis B pentavalent vaccination performed at the age of 6, 10 and 14 weeks in the DRC. Our 15.5% rate of non-response seems high compared with rates of <10% in studies of infants of similar age.[12-16]

Very few studies are available on the efficacy of hepatitis B vaccination in sub-Saharan Africa. In these studies, the first dose of vaccine was given after 4 weeks of age, and not at birth as recommended by the WHO. Nevertheless, our rate of seroprotection is lower than those found in previous studies in Gambia and South Africa (SA), which exceed 90%.[17,18] It is, however, higher than the rate of 80% found in a similar study in Ivory Coast.[19] It should be noted that in the SA study the investigators suggested that the seroprotection rate of 93% could be due to a highly immunogenic

Table 1. Characteristics of mothers and infants analysed in the study

Mothers	Infants
Sociodemographic variables	Characteristics of delivery
Medical history (parity, vaccine status)	Gender
Characteristics of pregnancy*	Number of vaccine doses
Educational status	Weight at birth
Serological status (HIV, HBsAg)	Serological status (HBsAb)

HBsAg = hepatitis B surface antigen; HBsAb = hepatitis B surface antibody.
*'Term' was defined as gestational age between 36 and 41 weeks, 'prematurity' as gestational age <36 weeks, and post-term pregnancy as gestational age >41 weeks.

vaccine and a decline in HBeAg seroprevalence as a consequence of several years of vaccination.[17]

In contrast to other reports, our study did not identify any maternal or intrinsic infant conditions associated with low immunological response. The mechanism of non-response to hepatitis B immunisation is still unknown, but factors associated with a low immune response rate are type of vaccine, age, male gender, obesity and smoking in healthy adults, and delayed administration, preterm birth, low birth weight and immunodeficiency in infants.[20,21] In our patients, no statistically significant differences in these variables were observed between the responders and the non-responders. Nevertheless, it must be noted that HBsAg and HBV DNA had not been tested before or at the time of hepatitis B vaccine administration. The possibility of an association between a certain type of HLA and impaired response has been suggested.[22,23] Liu *et al.*[24] found that non-response to hepatitis B vaccination in healthy Chinese individuals was associated with HLA B54. In Taiwan, Hsu *et al.*[25] reported that absence of response or low response was associated with over-expression of HLA-DR14-DR52. The possibility that our low response rate was due to intrinsic factors such as individual characteristics of our study population or malnutrition, which has been reported to impair response to vaccine,[8] cannot be excluded. Several years of war in our investigation area (South Kivu Province) had had numerous socioeconomic consequences, including malnutrition in children.

Table 2. General characteristics of the population of mothers (*N*=200)

	n (%)
Age (years)	
≤20	23 (11.5)
21 - 30	107 (53.5)
31 - 40	60 (30.0)
>40	10 (5.0)
Parity	
Primipara	4 (2.0)
2 - 5	191 (95.5)
Grand multipara (≥6)	5 (2.5)
Level of education	
No school	1 (0.5)
Primary school	43 (21.5)
Secondary school	110 (55.0)
Post-secondary school	46 (23.0)

Sub-Saharan countries represent a part of the world where hepatitis remains endemic and transmission frequently occurs *in utero*, during delivery or during the first years of life. Childhood immunisation therefore represents one of the goals of prevention of early-life transmission with its frequent chronic complications such as cirrhosis and hepatocellular carcinoma.[1,3] Many studies have demonstrated a dramatic reduction in the incidences of HBV infection and associated complications as a result of the programme of childhood immunisation.[6,20,21,26-29] For example, in Southern Italy, previously considered an area of very high endemicity, the prevalence of HBsAg declined from 13.4% to 0.9% after 20 years of implementation of the vaccination programme.[20] Immunisation of all infants is therefore one of the WHO's recommendations in the fight against HBV worldwide. Although these recommendations are based on the slight potential advantage in reduction of early transmission following a birth dose of vaccine, implementation of a birth dose is not always feasible in low-income countries for logistical and economic reasons.[8,18,30,31] In fact, only immunisation programmes with combined vaccines are currently sponsored by the WHO, and the monovalent vaccines (the only ones approved for use at birth) are not purchased by many African governments.[32] Only a few African countries have a hepatitis B vaccination programme with a birth dose (Nigeria, Gambia, Cape Verde), even if the first dose is not always given within 24 hours of birth as recommended, mainly for logistical and cultural reasons.[8] It must, however, be noted that no substantial difference in the response rate was reported in some studies comparing the immune response to hepatitis B vaccination given at birth or 4 or 6 weeks after delivery.[11,19,33,34]

Study limitations

Some limitations of this first study on HBV prevention in the DRC should be mentioned. These include the small size of our sample and the cross-sectional nature of the study. The latter in particular did not allow determination of middle/long-term protection. A prospective study could have identified the real rate of long-term protection, including slow responders. HBV DNA levels in the infants were not tested to identify occult HBV infection, and we did not determine maternal HBeAg/HBV DNA status. These factors should be taken into consideration when interpreting our findings. The relatively high rate of non-response in our study could in fact be related to some children having been infected prior to vaccination.[35] The switching from a quantitative to a qualitative anti-HBs test could also have affected our results, especially when interpreting borderline results with the qualitative test.

Table 3. Maternal and infant characteristics in responders and non-responders to hepatitis B vaccination

	Total (*N*=200)	Responders (*N*=169, 84.5%)	Non-responders (*N*=31, 15.5%)	*p*-value
Maternal characteristics				
Age (years), mean (SD) (95% CI)	29.3 (6) (26.3 - 30.9)	29.3 (5) (27.4 - 32.4)	29 (3.3) (26.7 - 31.3)	0.921
Parity, mean (SD) (95% CI)	3.4 (0.8) (3.33 - 3.55)	3.5 (0.5) (2.96 - 3.87)	3.38 (1.6) (3.34 - 3.57)	0.841
Duration of pregnancy (weeks), mean (SD) (95% CI)	37.9 (1.3) (37.7 - 38.0)	38 (1.5) (37.8 - 38.2)	37 (1.3) (36.6 - 37.5)	0.673
HIV-positive, *n* (%)	4 (2.0)	3 (1.8)	1 (3.2)	0.595
HBsAg-positive, *n* (%)	6 (3.0)	4 (2.4)	2 (6.4)	0.220
Infant characteristics				
Gender (F/M), *n*	107/93	90/ 79	17/ 14	0.870
Birth weight (g), mean (SD) (95% CI)	3.3 (0.4) (3.23 - 3.36)	3.3 (0.5) (3.26 - 3.39)	3.2 (0.3) (3.04 - 3.27)	0.546

SD = standard deviation; CI = confidence interval; HBsAg = hepatitis B surface antigen; F = female; M = male.

Conclusions

The study demonstrated that the rate of seroprotection after three doses of hepatitis B vaccine in Congolese infants is lower than desirable (>90%), but comparable to some data from other African countries with similar socioeconomic conditions. Further studies are needed to assess this finding and to evaluate ways to optimise the rate of seroprotection.

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1. Ganem D, Prince AM. Hepatitis B virus infection – natural history and clinical consequences. N Engl J Med 2004;350:1118-1129. https://doi.org/10.1056/NEJMra031087
2. World Health Organization. Global hepatitis report, 2017. http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/ (accessed 5 May 2017).
3. Oluyemi A, Odeghe E. Facing the challenges of hepatitis B management in a developing country. J Infect Dev Ctries 2012;6(3):299-300. https://doi.org/10.3855/jidc.2358
4. World Health Organization. Hepatitis B Fact Sheet. No. 204. Geneva: WHO, 2015. http://www.who.int/mediacentre/factsheets/fs204/en/ (accessed 15 July 2017).
5. Shepard CW, Simard EP, Finelli L, Fiore AE, Bell BP. Hepatitis B virus infection: Epidemiology and vaccination. Epidemiol Rev 2006;28(1):112-125. https://doi.org/10.1093/epirev/mxj009
6. Mast EE, Margolis HS, Fiore AE, et al.; Advisory Committee on Immunization Practices (ACIP). A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part I: Immunization of infants, children, and adolescents. MMWR Recomm Rep 2005;54(RR-16):1-31.
7. Expanded Programme on Immunization. Global Advisory Group – Part I. Wkly Epidemiol Rec 1992;67(3):11-15. https://apps.who.int/iris/handle/10665/228245 (accessed 1 April 2019).
8. Howell J, Lemoine M, Thursz M. Prevention of materno-foetal transmission of hepatitis B in sub-Saharan Africa: The evidence, current practice and future challenges. J Viral Hepat 2014;21(6):381-396. https://doi.org/10.1111/jvh.12263
9. Jack AD, Hall AJ, Maine N, Mendy M, Whittle HC. What level of hepatitis B antibody is protective? J Infect Dis 1999;179(2):489-492. https://doi.org/10.1086/314578
10. Plan Pluri Annuel Complet du PEV de la République Démocratique du Congo, 2015 - 2019. http://www.nationalplanningcycles.org/sites/default/files/country_docs/Democratic%20Republic%20of%20Congo/ppac_draft_1_rdc_2015-2019_va_gnm_input_hama_auga_02_02_2015_pm.pdf (accessed 21 September 2018).
11. Schillie SF, Murphy TV. Seroprotection after recombinant hepatitis B vaccination among newborn infants: A review. Vaccine 2013;31(21):2506-2516. https://doi.org/10.1016/j.vaccine.2012.12.012
12. Yates TA, Paranthaman K, Yu LM, et al. UK vaccination schedule: Persistence of immunity to hepatitis B in children vaccinated after perinatal exposure. Arch Dis Child 2013;98(6):429-433. https://doi.org/10.1136/archdischild-2012-302153
13. Hammitt LL, Hennessy TW, Fiore AE, et al. Hepatitis B immunity in children vaccinated with recombinant hepatitis B vaccine beginning at birth: A follow-up study at 15 years. Vaccine 2007;25(39-40):6958-6964. https://doi.org/10.1016/j.vaccine.2007.06.059
14. Jafarzadeh A, Montazerifar SJ. Persistence of anti-HBs antibody and immunological memory in children vaccinated with hepatitis B vaccine at birth. J Ayub Med Coll Abbottabad 2006;18(4):4-9.
15. Adkins JC, Wagstaff AJ. Recombinant hepatitis B vaccine: A review of its immunogenicity and protective efficacy against hepatitis B. Bio Drugs 1998;10(2):137-158. https://doi.org/10.2165/00063030-199810020-00005
16. Sanyal G, Shi L. A review of multiple approaches towards an improved hepatitis B vaccine. Expert Opin Ther Pat 2009;19(1):59-72. https://doi.org/10.1517/13543770802587226
17. Mphahlele MJ, Burnett RJ, Kyaw T, Schoeman HS, Aspinall S. Immunogenicity and safety of yeast-derived recombinant hepatitis B vaccine (Heberbiovac HB) in South African children. S Afr Med J 2004;94(4):280-281.
18. Viviani S, Carrieri P, Bah E, et al.; Gambia Hepatitis Intervention Study. 20 years into the Gambia Hepatitis Intervention Study: Assessment of initial hypotheses and prospects for evaluation of protective effectiveness against liver cancer. Cancer Epidemiol Biomarkers Prev 2008;17(11):3216-3223. https://doi.org/10.1158/1055-9965.EPI-08-0303
19. Ekra D, Herbinger KH, Konate S, et al. A non-randomized vaccine effectiveness trial of accelerated infant hepatitis B immunization schedules with a first dose at birth or age 6 weeks in Cote d'Ivoire. Vaccine 2008;26(22):2753-2761. https://doi.org/10.1016/j.vaccine.2008.03.018
20. Stroffolini T. The changing pattern of hepatitis B virus infection over the past three decades in Italy. Dig Liver Dis 2005;37(8):622-627. https://doi.org/10.1016/j.dld.2005.02.010
21. Centers for Disease Control. Progress in hepatitis B prevention through universal infant vaccination – China, 1997 - 2006. MMWR Morb Mortal Wkly Rep 2007;56:441-445.
22. Michel ML, Tiollais P. Hepatitis B vaccines: Protective efficacy and therapeutic potential. Pathol Biol 2010;58(4):288-295. https://doi.org/10.1016/j.patbio.2010.01.006
23. Hohler T, Reuss E, Evers N, et al. Diffential genetic determination of immune responsiveness to hepatitis B surface antigen and to hepatitis A virus: A vaccination study in twins. Lancet 2002;360(9338):991-995. https://doi.org/10.1016/S0140-6736(02)11083-X
24. Liu P, Xu H, Wang X, et al. Field epidemiological and experimental study on relationship between genetic factor and nonresponse or hyporesponse to hepatitis B vaccine. Chin Med J (Engl) 2000;113(6):547-550.
25. Hsu HY, Chang MH, Ho HN, et al. Association of HLA-DR14-DR-52 with low responsiveness to hepatitis B vaccine in Chinese residents in Taiwan. Vaccine 1993;11(14):1437-1440.
26. Simard EP, Miller JT, George PA, et al. Hepatitis B vaccination coverage levels among healthcare workers in the United States, 2002 - 2003. Infect Control Hosp Epidemiol 2007;28(7):783-790. https://doi.org/10.1086/518730
27. Chen H, Cantrell CR. Prevalence and factors associated with self-reported vaccination rates among US adults at high-risk of vaccine-preventable hepatitis. Curr Med Red Opin 2006;22(12):2489-2496. https://doi.org/10.1185/030079906X154088
28. Mast EE, Weinbaum CM, Fiore AE, et al.; Advisory Committee on Immunization Practices (ACIP). Prevention: A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: Immunization of adults. MMWR Recomm Rep 2006;55(RR-16):1-33.
29. Chang MH. Universal hepatitis B vaccination in Taiwan and the incidence of hepatocellular carcinoma in children. N Engl J Med 1997;336:1855-1859. https://doi.org/10.1056/NEJM199706263362602
30. Kim SY, Salomon JA, Goldie SJ. Economic evaluation of hepatitis B vaccination in low-income countries: Using cost-effectiveness affordability curves. Bull World Health Organ 2007;85:833-842. https://doi.org/10.2471/BLT.06.038893
31. Klingler C, Thoumi AI, Mrithinjayam VS. Cost-effectiveness analysis of an additional birth dose of hepatitis B vaccine to prevent perinatal transmission in a medical setting in Mozambique. Vaccine 2012;31(1):252-259. https://doi.org/10.1016/j.vaccine.2012.08.007
32. Lemoine M, Thursz MR. Battlefield against hepatitis B infection and HCC in Africa. J Hepatol 2017;66(3):645-654. https://doi.org/10.1016/j.jhep.2016.10.013
33. Del Canho R, Grosheide PM, Voogd M, Huisman WM, Heijtink RA, Schalm SW. Immunogenicity of 20 micrograms of recombinant DNA hepatitis B vaccine in healthy neonates: A comparison of three different vaccination schemes. J Med Virol 1993;41(1):30-34.
34. Agladioglu S, Beyazova U, Camurdan AD, Sahin, F, Atak, A. Immunogenicity of recombinant hepatitis B vaccine: Comparison of two different vaccination schedules. Infection 2010;38(4):269-273. https://doi.org/10.1007/s15010-010-0031-2
35. Zou H, Chen Y, Duan Z, Zhang H, Pan C. Virologic factors associated with failure to passive-active immunoprophylaxis in infants born to HBsAg-positive mothers. J Viral Hepat 2012;19(2):e18-e25. https://doi.org/10.1111/j.1365-2893.2011.01492.x

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